PATENT COOPERATION TREATY

From the INTERNATIONAL SEARCHING AUTHORITY

To: DUANE M. BYERS
NIXON & VANDERHYE P.C.
901 NORTH GLEBE ROAD, 11TH FLOOR
ARLINGTON, VA 22203-1808

PCT

INVITATION TO PAY ADDITIONAL FEES
AND, WHERE APPLICABLE, PROTEST FEE

(PCT Article 17(3)(a) and Rules 40.1 and 40.2(e))

Applicant's or agent's file reference DMB-4112-78	Date of mailing *(day/month/year)* PAYMENT DUE within **ONE MONTH** from the above date of mailing
International application No. PCT/US 08/12440	International filing date *(day/month/year)* 31 October 2008 (31.10.2008)
Applicant DIFFUSION PHARMACEUTICALS LLC	

1. This International Searching Authority

(i) considers that there are 11 *(number of)* inventions claimed in the international application covered by the claims indicated below/on an extra sheet:
Please see extra sheet

(ii) therefore considers that **the international application does not comply with the requirement of unity of invention** (Rules 13.1, 13.2 and 13.3) for the reasons indicated below/on an extra sheet:
Please see extra sheet

(iii) ☐ has carried out a partial international search (see Annex) ☒ will establish the international search report on those parts of the international application which relate to the invention first mentioned in claims Nos.:
1-7

(iv) will establish the international search report on the other parts of the international application only if, and to the extent to which, additional fees are paid.

2. Consequently, the applicant is hereby **invited to pay**, within the time limit indicated above, additional fees in the amount indicated below:

$1,800 (Fee per additional invention) x 10 (number of additional inventions) = $18,000 (total amount of additional fees/currency)

3. The applicant is informed that, according to Rule 40.2(c), **the payment of any additional fees may be made under protest**, that is, a reasoned statement to the effect that the international application complies with the requirement of unity of invention or that the amount of the required additional fees is excessive, where applicable, subject to the payment of a protest fee.

Where the applicant pays additional fees under protest, the applicant is hereby invited, within the time limit indicated above, to pay a protest fee (Rule 40.2(e)) in the amount of _____ *(amount/currency)*

Where the applicant has not, within the time limit indicated above, paid the required protest fee, the protest will be considered not to have been made and the International Searching Authority will so declare.

4. ☐ Claim(s) Nos. _____ have been found to be unsearchable under Article 17(2)(b) because of defects under Article 17(2)(a) and therefore have not been included with any invention.

Name and mailing address of the ISA/US Mail Stop PCT, Attn: ISA/US Commissioner for Patents P.O. Box 1450, Alexandria, Virginia 22313-1450 Facsimile No. 571-273-3201	Authorized officer: Lee W. Young PCT Helpdesk: 571-272-4300 PCT OSP: 571-272-7774

Form PCT/ISA/206 (April 2005)

RSA Search Fees Due 2/13/2009

Nixon & Vanderhye
Foreign Docketing

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Date of mailing *(day/month/year)*	JANUARY 13, 2009
Applicant's or agent's file reference: DMB-4112-78	PAYMENT DUE: within ONE MONTH from the above date of mailing
International application No.: PCT/US 08/12440	International filing date *(day/month/year)*: 31 October 2008 (31.10.2008)
Applicant: DIFFUSION PHARMACEUTICALS LLC	

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International application No.
PCT/US 08/12440

Continuation of Section 1:

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1. In order for all inventions to be examined, the appropriate additional examination fees must be paid.

Group I: claims 1-7, directed to a pharmaceutical composition comprising a diffusion enhancing compound.
Group II: claims 8, 10, 11, and 19-21, directed to a method for enhancing the diffusion of oxygen in a mammal and treating respiratory deficiencies or diseases using said enhanced diffusion of oxygen comprising administering a diffusion enhancing compound
Group III: claims 9, and 19-21, directed to a method of treating hemorrhagic shock comprising administering a diffusion enhancing compound.
Group IV: claims 12, 17 and 19-21, directed to a method of treating myocardial infarction, hypertension, ischemia or stroke comprising administering a diffusion enhancing compound.
Group V: claims 13 and 19-21, directed to a method of treating traumatic brain injury or Alzheimer's disease comprising administering a diffusion enhancing compound.
Group VI: claims 14 and 19-21, directed to a method of treating anemia comprising administering a diffusion enhancing compound.
Group VII: claims 15 and 19-21, directed to a method of treating chronic renal failure comprising administering a diffusion enhancing compound.
Group VIII: claims 16, 19-21, 23, 25 and 26, directed to a method of treating cancer comprising administering a diffusion enhancing compound.
Group IX: claims 18-21, directed to a method of treating diabetes and diabetes related complications comprising administering a diffusion enhancing compound.
Group X: claims 22, 25 and 26, directed to a method of treating Wegener's granulomatosis comprising administering a diffusion enhancing compound.
Group XI: claims 24-26, directed to a method of treating arthritis comprising administering a diffusion enhancing compound.

The inventions listed as Groups I - II do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:

The special technical feature of the Group I claims is a pharmaceutical composition comprising a diffusion enhancing compound. The special technical feature of the Group II-XI claims is the use of a preparation comprising a diffusion enhancing compound to treat a variety of individual diseases or conditions.

The only common technical element shared by the above groups is that they are related to the use of a diffusion enhancer in a pharmaceutical preparation. This common technical element does not represent an improvement over the prior art of the article entitled "Synergistic Effects of Chemical Enhancers and Therapeutic Ultrasound on Transdermal Drug Delivery" by Johnson et al. (see abstract). Therefore, the inventions of Groups I-XI lack unity of invention under PCT Rule 13 because they do not share a same or corresponding special technical feature.